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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/667,151	ZHONG ET AL.	
	Examiner	Art Unit	
	CHARLESWORTH RAE	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *22-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21, and 38-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 2/28/08, in response to the Office action, mailed 8/28/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

This action is made final.

Status of the Claims

Claims 1-39 are currently pending in this application.

Claims 22-37 are withdrawn for being directed to non-elected subject matter.

Claims 1-21 and 38-39 are under examination.

Response to applicant's arguments/remarks

Nonstatutory obviousness-type double patenting (ODP) rejections (see applicant's Response at page 7)

These rejections are maintained in view of applicant's non-response to the merits of the rejection as evidenced by applicant's statement requesting that the rejection be held in abeyance pending the disposition of the '828 copending application.

Rejection under 103(a) (see applicant's Response at pages 7-10):

Applicant contends that this rejection should be withdrawn for essentially the following summarized reasons (see applicant's Response at pages 7-10):

1) The combination of cited references fail to establish a prima facie case of obviousness.

2)Gentz et al. do not teach a chemical ablation agent in an amount effective to cause tissue necrosis.

3) The examiner has not offered any evidence to support the position that Gentz et al. discloses a chemical ablation in an amount effective to cause necrosis. The instant claimed formulation would be contrary to the basic teaching of Gentz of formulations for soft tissue growth regeneration.

4) One of ordinary skill in the art would not have been motivated to modify the formulation of Gentz to arrive at the instant claimed formulation.

5) The secondary references fail to remedy this deficiency. Neither Flaeke or Glajeh teaches a chemical ablation agent in art amount effective to cause tissue necrosis. Flacke was cited for purportedly teaching MKI contrast agents and Glajeh was cited for purportedly teaching ultrasound contrast agents.

In response, the rejection is maintained as applicant's arguments are not found to be persuasive for the reasons previously made of record in Office action, mailed 8/28/07, at pages 7-12 and for the additional reason(s) set forth below:

a) Gentz et al. teach sterile injectable formulations comprising sodium chloride (col 1. lines 19-24 and col. 4, line 11-67) i.e. the "a" component recited in claim 1. It is the examiner's position that it is within the scope of knowledge and skill of an artisan

skilled in the art to utilize sodium chloride in an effective amount to cause chemoablation of body tissue as evidenced by the teaching of Maguire et al. (US Patent 6,652,515) and Daellenbach (US Patent Application Pub. No. 2003/0163111 A1).

b) Gentz et al. teach sterile injectable formulations comprising thickening agents such as CMC and HPMC (col. 2, lines 3-7), which exemplifies applicant's "b" component recited in claim 1, for example.

c) To the extent that chemical ablation composition are known in the art, someone of skill in the art would have been motivated to combine the cited references relied upon in the rejections of record. Thus, someone of skill in the art at the time the instant invention was made would have deemed it obvious to create the instant claimed invention with reasonable predictability.

REJECTIONS

Nonstatutory Obviousness-Type Double-Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-21, and 38-39 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 40 in view of claims 1-39 of U.S. Co-pending US Patent Application No. 11/124,828 (Pub. No. 2006/0251581 A1; referred herein as Appl. No. '828). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are either anticipated by, or would have been obvious in view of the referenced claims.

Co-pending US Application No. 11/124,828/(Pub. No. 2006/0251581 A1; referred herein as McIntyre et al.) is directed towards a method for the treatment of uterine fibroids comprising providing an injectable or insertable formulation that comprises a

uterine fibroid treatment agent in an amount effective to cause shrinkage of uterine fibrinoids, and injecting or inserting said formulation into the uterine fibroid.

In particular, claim 40 of the reference copending application is directed towards a fibroid injectable or insertable formulation that comprises a uterine fibroid treatment, selected from a non-steroidal anti-inflammatory drug, an oral contraceptive, a GnRH agonist, an antiprogestogen, and a selective progesterone receptor modulator, in an amount effective to cause shrinkage of uterine fibroids. To the extent that the reference claim 40 does not provide a clear or precise definition of the terms "uterine fibroid," or "fibroid injectable or insertable formulation," or "amount effective to cause shrinkage of uterine fibroids," to reasonable interpret the claim, it is reasonable to use the reference specification as a dictionary to determine the meaning of the claim. McIntyre et al. define uterine fibroids, or uterine fibroid tumors, as non-cancerous smooth muscle tumors of the uterus (page 1, paragraph 0003, lines 1-3). McIntyre et al. disclose that uterine fibroid treatment agents for inclusion in the formulation of the invention include chemical ablation agents, whose inclusion in the formulations in effective amounts results in necrosis (death) or shrinkage of nearby tissue upon injection or insertion of the formulation into the tissue (page 2, paragraph 0022). McIntyre et al. disclose that in some embodiments, the injectable or insertable formulations of the invention are solids, semi-solids or high-viscosity fluids, which result in good dosage retention in the tissue, and thereby improving delivery efficiency of the treatment agents and/or minimizing the adverse effects such as unintended, nonspecific tissue damage (page 1, paragraph 0015). McIntyre et al. disclose that "high viscous" or "high viscosity" and other such

terms are used to describe fluids having viscosities greater than 1000 cps as measured by any number of techniques, including, for example, a Brookfield Kinematic Viscometer, model HBDV-II+CP with a CPE-40 cone spindle, set at 37 deegrees C. temperature, and using a 0.5 rpm speed setting (page 2, column 1, lines 7-12). Reference claims 1-39 are generally directed to methods/system for treating uterine fibroids comprising a) an injectable or insertable formulation that comprises a uterine treatment agent in an amount effective to cause shrinkage of uterine fibroids and b) an apparatus for injecting or inserting said formulation into said fibroids. Further, reference methods/system claims 1-39 encompass chemical ablation agents (e.g claims 1, and 14), biodisintegrable binders (e.g. claims 1, and 20), viscosity adjusting agents (e.g. claims 1, 26-28), alginate polymer (e.g. claims 1, and 34), and ionically crosslinked formulation (e.g. claims 1 and 33-34). Thus, the instant claimed invention and the reference invention are reasonably considered to be obvious variants of each other.

Thus, claims 1-21, and 38-39 are deemed to be obvious variants of the limitations of reference claim 40 in view of reference claims 1-39.

This is a provisional obviousness-type double patenting rejection because the conflicting claims of the copending applications have not in fact been patented.

Claim rejections – 35 USC 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13, 19-21, and 38-39 are rejected as being unpatentable over Gentz et al. (US Patent 6,869,927 B1).

Gentz et al. teach liquid injectable formulations of keratinoycte growth factor-2 (KGF-2) and derivatives thereof (column 1, lines 19-24, and column 4, line 11-67), comprising KGF-2 polypeptides and sodium chloride as a tonicifier at a concentration of from about 0 to about 150 mM (NACl) (column 4, line 34). Sodium chloride of about 150 mM is reasonably construed to serve as a chemical ablation agent in amount effective to cause tissue necrosis and to reasonably serve as a biodisintegrable viscosity adjusting agent in an amount effective to render the formulation highly viscous (see instant specification, page 3, paragraph 0019, line 1 to paragraph 0020, line 2; and page 5, paragraph 0026). Gentz et al. teach that the KGF-2 to be used for therapeutic administration may be sterile and that sterility is readily accomplished by filtration through sterile filtration membranes (column 14,

lines 33-35). Sodium chloride is reasonably construed to be an osmotic-stress-generating agent in view of applicant's disclosure that "[I]n some embodiments, the ablation agents are osmotic-stress-generating agents, for example, a salt, such as sodium chloride (page 3, paragraph 0020, lines 1-2)." Gentz et al. teach that the formulations may employ "suitable pharmaceutical diluents," including but not limited to, saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof (column 12, lines 29-34). "Suitable pharmaceutical diluents ....and combination thereof" is reasonably construed to encompass an amount of water and ethanol suitable for the preparation of a sterile injectable formulation as claimed in the instant application (specification page 5, lines 1-2). . Gentz et al. teach that thickenening agents are used to increase the viscosity of the formulation e.g. carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), hydroxypropylmethyl cellulose (HPMC), natrosol, and carbomers (column 2, lines 3-7). Gentz et al. teach examples of etherified cellulose to include alkyl celluloses e.g. methylcellulose, hydroxyethyl cellulose, hydroxyl propyl cellulose, hydroxyl propyl methylcellulose, and the like (column 9, lines 5-9). Gentz et al. teach that when thickening agents are added to the injectable formulations, salts and buffering agents may be added or removed from the formulation for optimal stability (column 9, second paragraph, lines 1-3). Gentz et al. teach that gelling agents may be added to the injectable formulations, including vinyl polymers, polyoxyethylenepolyoxypropylene copolymers, polysaccharides, proteins, poly(ethylene oxide), acrylamide polymers and derivatives and salts thereof; useful polysaccharides include cellulose

derivatives, glycosaminoglycans, agar, pectin, alginic acid, dextran, starch, and chitosan (column 10, lines 19-51). Based on this teaching, ionically cross-linkable polymers such as alginate polymer are reasonably within the capabilities of someone of skill in the art. Gentz et al. teach that additional stabilizing agents may be added to the formulation, including anionic and polyanionic species [heparin analogs] (column 11, line 65 to column 12, line 27). Gentz et al teach that the formulations are prepared contacting the KGF-2 polypeptide uniformly and intimately with liquid carriers or finely divided solid carriers or both (column 13, lines 63-65). Gentz et al. also teach that the carrier may also contain minor amounts of suitable additives such as substances that enhance isotonicity and chemical stability e.g. phosphate, citrate, succinate, acetic acid, and other organic acids or their salts; antioxidants such as ascorbic acid; low molecular weight polypeptides e.g. polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; ... (column 14, lines 9-25). Gentz et al. teach high molecular weight polymers of acrylic acid cross-linked with either allyl ethers of pentaerythritol (column 9, lines 1-5). Gentz et al. teach that the thickening agent should raise the viscosity to about 50 to about 10,000 centipoise (cps); the viscosity is measured using a rotating spindle viscometer (column 8, last paragraph, last paragraph). The term "about 10,000" is reasonable construed to overlap with the instant claimed limitation of "from 5,000 cps to 100,000 cps" and "from 10,000 cps to 50,000 cps." Gentz et al. disclosed formulations reasonably

encompass injectable formulations comprising a plurality of ablation agents. For example, reference claim 72, is directed toward a composition comprising a polypeptide, hydroxymetylcellulose, sucrose, sodium citrate, sodium chloride, and EDTA. To the extent that reference claim 72 recites the term "comprising," it is reasonable to construe the reference claim as contemplating the addition of other ablation agents and additional viscosity adjusting agents besides sodium chloride, which reasonably satisfies the "plurality of viscosity adjusting agent" and "plurality of ablation agents" limitations.

Thus, based on the teaching of Gentz et al., someone of skill in the art would have been motivated to create the instant claimed inventive concept. Thus, someone of skill in the art at the time the instant claimed invention was made to create the instant invention with a reasonable predictability in view of the general knowledge of the state of the art.

Rejection under 103

Claims 14-18 are rejected as being unpatentable over Gentz et al (US Patent 6,869,927 B1), in view of Flacke et al. (Novel MRI contrast agent for molecular imaging of fibrin –implications for detecting vulnerable plaques. Circulation. 2001;104:1280-1285), in view of Glajch et al. (US Patent 5,147,631).

The above discussion of Gentz et al. is incorporated by reference. It is noted that Gentz et al. do not teach imaging contrast agent.

Flacke et al. is added for its general teaching of contrast agents. Flacke et al. teach a fibrin-specific MR contrast agent that could allow enhanced, sensitive detection and quantification of occult microthrombi within the intimal surface of atherosclerotic vessels in symptomatic patients and provide direct evidence to support acute therapeutic intervention (page 1280, last paragraph, line 1 to page 12 81, line 6).

Glajch et al. is added to show the general knowledge in the art regarding formulations comprising contrast agents, polymers, and solid particles. Glach et al. teach ultrasound contrast agents comprising porous particles of an inorganic material having an average particle diameter of about 0.05 to 500 microns and containing entrapped gas or liquid; the inorganic material includes monomeric and polymeric forms of one or more of the following: borates, aluminas, carbonates, silicates, silicas, aluminosilicates, phosphates, and organic or inorganic cationic salts thereof (column 2, lines 11-27). This teaching is reasonably construed to satisfy the "wherein the plurality of solid particles is selected from calcium carbonate particles ..." instant claim limitation. For parenteral use, the particles are preferably about 0.2-10 microns in average diameter (column 2, lines 33-34). Glajch et al. teach that these contrast agents are useful for ultrasound imaging of a body organ system (column 2, lines 66-68).

Based on the teaching of Glajch et al. of ultrasound contrast agents useful for ultrasound imaging of a body organ system, someone of skill in the art would have been motivated to combine the teachings of the above cited references to arrive at the instant claimed invention. Thus, someone of skill in the art would have deemed it obvious at the

time the instant invention was made to create the instant invention with a reasonable predictability.

For the above reasons, someone of skill in the art would have deemed it obvious to create the instant invention with a reasonable expectation of success in view of

Relevant Art of Record

The below cited art references made of record and relied upon are considered pertinent to applicant's invention.

Maguire et al. (US Patent 6,652,515) teach a system and method that treats atrial arrhythmia by ablating a circumferential region of tissue (col. 2, lines 40-65; col. 17, lines 38-48; and col. 18, lines 16-32). In particular, Maguire et al. teach a fluid ablation element that supply radiofrequency or other mode of electrical current to the tissue by electrically coupling an electrical abalation element to the tissue via an ablation medium which is an electrically conductive fluid, such as for example an ionic fluid which may, in one illustraive variation, hypertonic saline (co. 18, lines 16-32, especially lines 24-30). Maguire et al. teach fluid ablation element wherein the said fluid ablation element infuse the ablation medium, such as a fluid containing alcohol, directly into the tissue in order to substantially alter the nature of that tissue (col. 18, lines 16 to 24).

Daellenbach (US Patent Application Pub. No. 2003/0163111 A1) teach that chemical ablation creates linear patterns of scar tissue that block electrical pathways by the introduction of a toxic chemical such as hypertonic saline, ethanol or formaldehyde (para 0050). Daellenbach teaches a method for delivering a fluid into an internal organ of a living organism comprising inserting a first part of a needle-free injection system

wherein then system injects a fluid through an orifice and into the internal organ such that the fluid penetrates the organ without destroying the functionality of the organ (para 0008). Daellenbach disclose 15 % hypertonic saline injection fluid for injection into the pericardium of a dog (para 0052).

Feng (US Patent Application Pub. No. 2005/0048132 A1) teach a method of suing hydrochloric acid injections for tumorous tissue coagulation and necrosis, including beningn tumors (abstract).

Escandon et al. (US Patent Application Pub. No. 2003/0092689 A1) teach methods for treating diseased prostate tissue, including the steps of chemically ablating prostate tissue and coadministering an antiandrogen, wherein the prostate tissue is chemically ablated by injection of ethanol, or an injectable gel comprising ethanol, into prostate tissue (abstract; and col 4, lines 1-36).

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http:pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 800-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

2 June 2008

/C. R./
Examiner, Art Unit 1611

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614